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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/606,804	06/28/2000	Amy S. Lee	06666-040001	5664

20985 7590 10/02/2002

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EXAMINER	
WHITEMAN, BRIAN A	
ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 10/02/2002 9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/606,804	Applicant(s) LEE, AMY S.	
	Examiner Brian Whiteman	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-62 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-62 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-62 are pending.

Claim 38 is not a proper linking claim between claims 42 and 44 because the method of treating a cell proliferative disorder in a subject comprising administering a nucleic acid from claim 1 or 22 is an in vivo method of gene therapy and is distinct from an ex vivo method of gene therapy comprising administering a genetically modified cell comprising the nucleic acid of claim 1 or 22. In view of the specification, an ex vivo method is distinct from an in vivo method and claim 38 is not considered a generic claim linking claims 42 and 44.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121 and election of species is required under 35 U.S.C. 121:

I. Claims 1-16, 18-43, 45-46, drawn to a nucleic acid construct comprising at least one stress responsive non-coding regulatory sequence comprising at least two endoplasmic reticulum stress elements (ERSE) as set forth in SEQ ID NO: 1, and a heterologous nucleic acid sequence operatively linked to the regulatory sequence and wherein the heterologous sequence encodes a therapeutic agent effective for treating a cell proliferative disorder, a nucleic acid construct comprising at least one stress responsive non-coding regulatory sequence comprising at least two endoplasmic reticulum stress elements (ERSE) as set forth in SEQ ID NO: 1, and a heterologous nucleic acid sequence operatively linked to the regulatory sequence and wherein the heterologous sequence encodes a therapeutic agent effective for treating a disorder associated with glucose

starvation; a method for inhibiting cell proliferative disorder in a subject using the nucleic acid construct of claim 1 or claim 22, classifiable in class 435, subclass 320.1; class 514, subclass 44.

II. Claims 17, 36, and 47, a nucleic acid construct comprising at least one stress responsive non-coding regulatory sequence comprising at least two endoplasmic reticulum stress elements (ERSE) as set forth in SEQ ID NO: 1, and a heterologous nucleic acid sequence operatively linked to the regulatory sequence and wherein the heterologous sequence encodes a detectable marker; a method for detecting cell proliferative disorder in a subject using the nucleic acid construct of claim 17, class 424, subclass 9.1.

III. Claims 44, drawn to an *ex vivo* method for treating a cell proliferative disorder in a subject comprising administering to the subject a nucleic acid of claim 1 or 22, class 424, subclass 93.2.

IV. Claims 48-62, drawn to a transgenic non-human animal or transgenic non-human cell comprising the nucleic acid construct in claims 1, 17, 22; and a method of producing the non-human transgenic animal, classifiable in class 800, subclass 8.

If applicants elect group IV, applicants are further required to elect from the following groups:

a.) A detectable marker; or

b.) A heterologous nucleic acid sequence encoding a therapeutic agent effective for treating a cell proliferative disorder.

In addition, if applicants elect group b), applicants are further required to elect a distinct heterologous nucleic acid set forth on pages 21-26 in the specification.

The inventions are distinct, each from the other because of the following reasons:

As set forth in *In re Harnisch* (631F.2d 716 206 USPQ 300 (CCPA 1980), see MPEP 803.02, unity of invention exists for all species in a claim (1) shows a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility.

In view of *In re Harnisch*, claims 1-62 lack unity of invention for the following reasons: 1) an *ex vivo* method and *in vivo* method of inhibiting cell proliferation, 2) a therapeutic agent and a detectable marker. An in vivo method of gene therapy does not have a common utility with an ex vivo method and neither method shares a substantial structural feature disclosed as being essential for that utility. In addition, a therapeutic agent and a detectable marker do not have a common utility and share a substantial structural feature disclosed as being essential for that utility. A transgenic non-human animal with a detectable marker does share a substantial structural feature with a transgenic animal with a heterologous nucleic acid encoding a therapeutic protein. Furthermore, a transgenic animal comprising a specific heterologous nucleic acid sequence encoding a therapeutic agent effective for treating a cell proliferative disorder does not share a substantial structural feature disclosed as being essential to the that utility with a transgenic animal comprising a distinct heterologous nucleic acid sequence. For example a transgenic animal comprising a pro-drug does not share a substantial structural feature as a transgenic animal comprising a heterologous gene encoding p53 protein. Therefore in view of In re Harnisch, claims 1-62 lack unity of invention and are separated into distinct groups as shown in Group I-IV.

Inventions I, II, and IV, are distinct. Inventions are distinct if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, invention I is directed to a nucleic acid comprising a heterologous nucleic acid sequence; Invention II is directed to a nucleic acid comprising a heterologous nucleic acid encoding a detectable marker; and invention IV is directed to transgenic non-human animals comprising a heterologous sequence encodes a therapeutic agent effective for treating a cell proliferative disorder or a transgenic non-human animals comprising a detectable marker. The inventions are distinct because they are not capable of use together and they have different modes of operation or different functions. The method set forth in claim 36 is separated into Group I and II because the method in claim 36 uses distinct nucleic acid constructs and it is not apparent what is the nexus between the pre-amble and the body of claim 36. Furthermore, the method does not define whether the nucleic acid being increased is an exogenous nucleic acid or an endogenous nucleic acid and Invention II uses a detectable marker that is non-therapeutic and Invention I encompasses a nucleic acid encoding a therapeutic protein. Invention I is directed to using a nucleic acid in a therapeutic method as set forth in claims 36-38; invention II is directed to using a nucleic acid to detect whether a subject has cancer or is pre-disposed to cancer as in claim 47. The different between inventions I, II, and IV are further underscored by their different classification and independent search status.

Although there are no provisions under the section for "Relationship of Inventions" in MPEP 806.05 for inventive groups that are directed to <u>different</u> methods. MPEP 802.01 states, "35 U.S.C. 121 quoted in the preceding section states that the Commissioner may require

restriction if two or more "independent and distinct" inventions are claimed in one application. Thus, a restriction is deemed to be proper because each of the methods of inventions I-IV constitutes patentably distinct inventions for the following reasons: Each of the inventions is directed to different goals and comprises materially distinct steps, wherein each of the compositions in each invention is structurally distinct and/or generates distinct mechanisms and functional effects as indicated above. The scope of each of the cited inventions encompasses an employed method, which generates distinct function(s) and effect(s), and furthermore does not necessarily overlap with that of another invention. For example, the method steps of Group II are distinct and are not encompassed by Groups I, III, or IV because a method of detecting a cell proliferative disease in a subject requires distinct method steps than the methods steps used in Groups I, III, or IV. Each of the inventions I-IV comprises materially distinct steps, and/or generates different functions and effects, and thus, is not required for use with one another.

If applicant elects Group I, this group contains claims directed to the following patentably distinct species of the claimed invention: in vivo administration is by systemic, local, or topical administration in claim 43.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claim 42 generic.

Furthermore, if applicant elects Group I, either of these groups contain claims directed to the following patentably distinct species of the claimed invention: neoplastic disorder in claim 46.

Applicant is further required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claim 45 generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

If applicant elects Group I, claims 1 is generic to a plurality of disclosed patentably distinct species comprising therapeutic agent selected from a biologically active protein is an enzyme in claim 6, antisense RNA in claim 10, or tumor suppressor protein in claim 13. Applicant is also required under 35 U.S.C. 121 to elect a single disclosed species, even though this requirement is traversed.

Furthermore if applicants elect enzyme in claim 6, claim 6 is generic to a plurality of disclosed patentably distinct species comprising enzymes listed in claim 8. Applicant is also required under 35 U.S.C. 121 to elect a single disclosed species, even though this requirement is traversed.

If applicants elect anti-sense RNA in claim 10, claim 10 is generic to a plurality of disclosed patentably distinct species comprising oncogenes listed in claim 12. Applicant is further required under 35 U.S.C. 121 to elect a single disclosed species, even though this requirement is traversed.

However, if applicants elect tumor suppressor protein in claim 13, claim 13 is generic to a plurality of disclosed patentably distinct species comprising tumor suppressor protein listed in claim 14. Applicant is further required under 35 U.S.C. 121 to elect a single disclosed species, even though this requirement is traversed.

Claim 28 is generic to a plurality of disclosed patentably distinct species comprising viral vectors listed in claim 29. Applicant is also required under 35 U.S.C. 121 to elect a single disclosed species, even though this requirement is traversed.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Because these inventions are distinct for the reasons given above and the literature search required for each Group is not required for any other Group, restriction for examination purposes as indicated is proper.

It would be unduly burdensome for the examiner to search and consider patentability of all of the presently pending claims, a restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 § 1.17(h).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kay Pinkney whose telephone number is (703) 305-3553.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775.

The examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, primary examiner, Dave Nguyen can be reached at (703) 305-2024.

If attempts to reach the primary examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader, SPE - Art Unit 1635, can be reached at (703) 308-0447.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Brian Whiteman
1635
9/30/02

DAVE T. NGUYEN
PRIMARY EXAMINER